CLAIMS

1. A T cell receptor (TCR) molecule containing an alpha chain portion and a beta chain portion wherein the alpha chain portion contains three complementarity determining regions (CDRs):
CDR1α: SSYSPS
CDR2α: YTSAATL
CDR3α: VVSPFSGGGADGLT or comprising or consisting of SPFSGGGADGLT
and the beta chain portion contains three complementarity determining regions (CDRs):
CDR1β: DFQATT
CDR2β: SNEGSKA
CDR3β: comprising SARDGGEG or comprising or consisting of RDGGEGSETQY, or wherein up to three amino acid residues in one or more of the CDRs are replaced by another amino acid residue.

2. A TCR molecule according to Claim 1 wherein CDR3α has the amino acid sequence VVSPFSGGGADGLT.

3. A TCR molecule according to Claim 1 wherein the CDR3α has the amino acid sequence SPFSGGGADGLT.

4. A TCR molecule according to Claim 1 wherein the CDR3β has the amino acid sequence SARDGGEG.

5. A TCR molecule according to Claim 1 wherein the CDR3β has the amino acid sequence RDGGEGSETQY.

6. A TCR molecule according to any one of the preceding claims wherein the alpha chain portion and the beta chain portion are present on different polypeptide chains.

7. A TCR molecule according to any one of Claims 1 to 5 wherein the alpha chain portion and the beta chain portion are present in the same polypeptide chain.

8. A TCR molecule according to any of Claims 1 to 7 wherein the CDRs are grafted to a human framework region.

9. A TCR molecule according to Claim 8 wherein the alpha chain portion has the amino acid sequence given in Figure 2.

10. A TCR molecule according to Claims 8 or 9 wherein the beta chain portion has the amino acid sequence given in Figure 4.

11. A TCR molecule according to any one of Claims 1 to 10 which is soluble.

12. A polynucleotide encoding the alpha chain portion as defined in Claim 1.

13. A polynucleotide encoding the beta chain portion as defined in Claim 1.

14. A polynucleotide encoding the single chain TCR molecule as defined in Claim 7.

15. An expression vector comprising a polynucleotide according to any of Claims 12 to 15.

16. An expression vector according to Claim 15 which is a retroviral vector.

17. A host cell comprising a polynucleotide according to any of Claims 12 to 14 or an expression vector according to Claims 15 or 16.

18. A host cell according to Claim 17 which is a T cell.

19. A host cell according to Claim 18 which is a T cell derived from a patient.

20. A method of combating a WT1-expressing malignancy in a patient, the method comprising introducing into the patient a T cell, preferably derived from the patient, which is modified to express the TCR molecule of any of Claims 1 to 11.

21. A method according to Claim 20 comprising (1) obtaining T cells from the patient, (2) introducing into the T cells a polynucleotide according to any of Claims 12 to 14 or an expression vector according to Claims 15 or 16 so that the T cell expresses the encoded TCR molecule and (3) introducing the cells from step (2) into the patient.

22. A method according to Claim 20 or 21 wherein the WT1-malignancy is any one or more of breast cancer, colon cancer, lung cancer, leukaemia, ovarian cancer, melanoma, head and neck cancer, thyroid cancer, glioblastoma and sarcoma.

23. Use of a T cell, preferably a patient derived T cell, modified to express the TCR molecule of any of Claims 1 to 11 in the manufacture of a medicament for combating a WT1-expressing malignancy in the patient.

24. Use according to Claim 23 wherein a polynucleotide according to any of Claims 12 to 14 or an expression vector according to Claims 15 or 16 has been introduced into the T cell, preferably patient derived T cell, so that the T cell expresses the encoded TCR molecule.

25. A method of selecting a TCR molecule with improved binding to an HLA-A2/RMFPNAPYL complex comprising (a) providing a TCR molecule containing an alpha chain portion and a beta chain portion wherein the alpha chain portion contains three complementarity determining regions

(CDRs):
CDR1α: SSYSPS
CDR2α: YTSAATL
CDR3α: VVSPFSGGGADGLT or comprising or consisting of SPFSGGGADGLT
and the beta chain portion contains three complementarity determining regions (CDRs):
CDR1β: DFQATT
CDR2β: SNEGSKA
CDR3β: comprising SARDGGEG or comprising or consisting of RDGGEGSETQY.

wherein at least one amino acid residue in one or more of the CDRs as given is replaced with another amino acid residue, (b) determining whether the TCR molecule binds to an HLA-A2/RFMPNAPYL complex with greater affinity than a TCR molecule without the replacement amino acid(s), and (c) selecting a molecule which binds with greater affinity.

26. A method according to Claim 25 wherein the CDR3s are as defined in any of Claims 2 to 9.

27. Any novel method of combating cancer as herein described.